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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,329	03/31/2004	Arlindo L. Castelhano	60390-AZ-PCT-US/JPW/GJG/J	9147

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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/816,329	CASTELHANO ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,11,12,22,23 and 187-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,11,12,23 and 187-189* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/728,229.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/31/04 & 4/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

S.O.O.

DETAILED ACTION

1. This action is in response to an application filed on 3/3/04. There are eight claims pending and eight under consideration. Claims 11, 12, 22, 23, and 187-189 are compound claims. Claim 5 is a method of using claim. This is the first action on the merits. The application concerns some 2-phenyl-4-heterocyclo-pyrrolo[2,3-d]pyrimidine compounds and uses thereof.

Priority

2. The status of non-provisional parent application should also be included. Since the parent application has become a patent, please update the first line of the specification with the expression "now Patent No. 6,800,633" following the filing date of the parent application.

Title

3. The title of the invention is no longer descriptive after restriction. A new title is required that is clearly indicative of the invention to which the claims are directed. The following is suggested: adding the phrase "4-Heterocyclo-" before the word "Pyrrolo".

Abstract

4. Applicant is reminded of the proper content of an abstract of the disclosure. A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. In chemical patent abstracts for compounds or compositions, the general nature of the

compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The abstract is too short and generic. Examiner suggests claim 11, including the figure, and the utility.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating any human disease. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the

predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The five main issues are the lack of any correlation between clinical efficacy for treatment of the twelve diseases and Applicants' four *in vitro* assay, the limited biological testing done upon compounds within the scope of formula (I), the state of the prior art, the complete lack of skill of clinicians in using A1 agonists in treating disease, and the breadth of the claims.

There is an *in vitro* assay, drawn to binding to a human A1 receptor expressed in yeast, described in lines 9-22, page 105 with data on compound CDS-116676 only. There is an *in vitro* assay, drawn to binding to a human A2a receptor expressed in yeast, described in the passage spanning line 24, page 105 to line 4, page 106 with data on compound CDS-116676 only. There is an *in vitro* assay, drawn to binding to a human A2b receptor expressed in yeast, described in the passage spanning line 26, page 106 to line 16, page 107 with data on compound CDS-116676 only. There is an *in vitro* assay, drawn to binding to a human A3 receptor expressed in yeast, described in lines 6-24, page 106 with data on compound CDS-116676 only. There is data on compounds found in pages 109-124. Of all these compounds on one, CDS-116676, on page 122 fits the limitations of the present formula I. Applicants do not state and it is not recognized in the

clinical arts this assay is correlated to clinical efficacy for the treatment of any of the claimed diseases. Although Applicants have established that this compound binds to the four receptors, they have not established if the compound is an agonist or an antagonist at any or all of these receptors.

The state of the clinical arts in adenosine-receptor related diseases is provided by Yan (Expert Opinion on Emerging Drugs). Yan (Expert Opinion on Emerging Drugs) states in his conclusion on page 555 that the only art-recognized uses of A_1 and A_{2A} agonists are controlling arrhythmia and heart diagnosis. Unfortunately, Applicants claim neither indication. The use of GW-493838 for treating pain is discussed in the same paragraph. Unfortunately, Applicants do not claim the treatment of pain. Baraldi (Expert Opinion on Therapeutic Patents, 2004) states in the first complete paragraph, page 77 in his conclusion that with A_1 agents "efficacy has yet to be shown". Baraldi (Expert Opinion on Therapeutic Patents, 1999) states in the final paragraph on page 524, "[t]he different effects of A_3 receptor agonists *in vitro* and *in vivo* are still not clear".

The lack of skill of clinical practioners with using A_1 agents is made clear in the first complete paragraph on page 555 of Yan (Expert Opinion on Emerging Drugs).

The scope of the claims involves all of the thousands of compounds of claim 11 as well as the unknown list of diseases embraced by the term neutrophil chemotaxis. Thus, the scope of claims is broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used

to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5, 11, 12, 23, and 187-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4-5, 8, 9, 12, 29, and 33 of U.S. Patent No. 6,664,252. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound of claim 9 of U.S. Patent No. 6,664,252 fits formula (I) with $R_1 = R_2$ = pyrrolidine substituted by hydroxymethylene, R_3 = phenyl, and $R_4 = R_5 = R_6$ = H. Claim 8 of U.S. Patent No. 6,664,252 has an acetoamido group on the pyrrolidine substituent. Thus, the present claim 23 is made obvious. This is a species/genus situation. According to the MPEP §806.04(i) "Generic Claims Presented for First Time After Issue of Species. The Office no longer follows the practice of prohibiting the allowance of generic claims that are presented for the first time after the issuance of a copending application claiming plural species. Instead, the Office may reject the generic claims on the grounds of obviousness-

type double patenting. Applicant may overcome such a rejection by filing a terminal disclaimer. See *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29."

7. Claims 5, 11, 12, 23, and 187-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 10, 14, 16, 29-31, and 35-37 of U.S. Patent No. 6,680,324. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound of claim 9 of U.S. Patent No. 6,664,252 fits formula (I) with $R_1 = R_2$ = pyrrolidine substituted by acetoamido, R_3 = phenyl, and $R_4 = R_5 = R_6$ = H. This is a species/genus situation. According to the MPEP §806.04(i) "Generic Claims Presented for First Time After Issue of Species. The Office no longer follows the practice of prohibiting the allowance of generic claims that are presented for the first time after the issuance of a copending application claiming plural species. Instead, the Office may reject the generic claims on the grounds of obviousness-type double patenting. Applicant may overcome such a rejection by filing a terminal disclaimer. See *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29."

8. Claims 5, 11, 12, and 187-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 11-14, and 16 of U.S. Patent No. 6,800,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because in claims 1

and 2 of U.S. Patent No. 6,800,633 R_1 and R_2 as one possibility among a dozen choices can form a heterocyclic ring as required by the present claims. The definitions of R_3-R_6 are the same in both sets of claims. The guidance to choose R_1 = R_2 = pyrrolidine substituted by acetoamido is found in columns 89-90, final entry with compound CDS-116676.

9. U.S. Patent No. 6,800,633 is the parent of the present application and normally cannot be the basis of a double patenting rejection because there was a restriction issued in that parent application. However, there is an exception to this rule provided in MPEP §804.01 (B) when "[t]he claims of the different applications or patents are not consonant with the restriction requirement made by the examiner". Such is the case here. Group IV of the restriction made in the parent case provided for compounds where R_1 and R_2 form a heterocyclic ring. This is the present definition of these two variables. As pointed out above, such compounds are also included in the claims of U.S. Patent No. 6,800,633.

Allowable Subject Matter

10. Claim 22 IS objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

11. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624
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TCMcK/me